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SCHOOL OF AEROSPACE MEDICINE
USAF AEROSPACE MEDICAL CENTER (ATC)
BROOKS AIR FORCE BASE, TEXAS

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PRODUCTION OF GAS IN HUMAN TISSUES AT LOW PRESSURES

The development of a gas phase in human tissues was studied by exposing the left hand of each of 6 volunteer subjects to a total pressure of 49 mm. Hg or less. A gas pocket which developed in the hands of 4 of the subjects was clearly discernible by visual inspection and an appropriate roentgenographic technic. The gas pocket developed at chamber pressures less than 26 mm. Hg (23.2 km.) on initial exposure and disappeared at a chamber pressure greater than 226 mm. Hg (9.2 km.). The swelling was never painful, always disappeared promptly on repressurization of the chamber, and has never caused any apparent temporary or permanent injury to the hand. Subsequent exposure of the hand to a low total pressure caused swelling at 70 mm. Hg or more. Carbon dioxide and water vapor are believed to be the main gases involved in the phenomenon.

A satisfactory plethysmograph was developed and used in this research project in studying the change in volume of the human hand at extreme chamber pressures.

STATEMENT OF THE PROBLEM

Modern man pursues a continuing technologic struggle to master his immediate environment and to extend his manifest destiny toward other planets and other solar systems. During the present century he has used aircraft and rocket-launched satellites in this conquest. As a result of this research he has gained a better understanding of the earth's atmosphere and of the envelope of space beyond that atmosphere. He is discovering that environments of the upper atmosphere and of space are hostile and, in these environments, he must take special precautions to protect himself. One of the threats to his safety during exploration of the upper atmosphere is that of exposure to extremely low barometric pressures. He knows that a very low ambient pressure will not support human life. It becomes necessary to study the reaction of human and other living tissues exposed to low pressures so that man may devise and perfect the necessary protective equipment which will enable him to continue this vitally important conquest.

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This research project was designed to find answers to the following questions:

1. At what total pressure does gas develop in the hand of a denitrogenated subject?

2. Once the gas develops, at what total pressure does it disappear?

3. Will the gas always develop and subside at the same pressure?

4. What are the volumetric changes in the human hand during the development of gas?

5. Can a plethysmograph be developed which will reliably and accurately measure volume changes in the human hand at total pressures as low as 3 mm. Hg?

6. Can roentgenographic technics be used to demonstrate the development and disappearance of the gas?

7. Is there a significant change in the blood pressure in the arm of the exposed hand?

8. In a followup study, is there temporary or permanent injury to the human hand which has been experimentally exposed to a total pressure of 3 mm. Hg?

9. Can one deduce, from experimental observations, the probable nature of the evolved gas?

BACKGROUND OF THE PROBLEM

The combined genius of three seventeenth-century scientists has provided succeeding generations of mankind with the necessary tools for studying the effects of greatly reduced barometric pressures on living organisms. Torricelli devised a mercury barometer in 1643 and through a careful series of experiments demonstrated that the earth's atmosphere has weight and exerts a pressure (14). He was aware of the presence of a vacuum in the space above the mercury column and observed that tiny snails, leeches, and insects died in the vacuum. He had difficulty deciding whether the deaths were due to the vacuum or to injury from the mercury (1, 7). Several of his colleagues (Accademia del Cimento) expanded Torricelli's research on animals. They observed that birds, reptiles, and smaller insect and aquatic forms died in a vacuum (1, 7).

Otto von Guericke of Prussia conducted a series of related experiments beginning about 1632. He invented a metal syringe and initially used it in an attempt to evacuate water from a sealed wooden cask. In later experiments (23) he discovered that when gas was evacuated from a rigid copper sphere the great atmospheric pressure outside it suddenly and dramatically crushed the sphere. In his most famous demonstration Von Guericke employed two rigid metal hemispheres which were held together by atmospheric pressure. He demonstrated that two teams of eight horses each could not pull apart the evacuated hemispheres.

Robert Boyle was aware of the work of Torricelli and of Von Guericke. Boyle's major contributions were the development of refined vacuum pumps (he was able to produce a vacuum of 6 mm. Hg); a thorough investigation into the relationship between barometric pressure exerted on a gas and the volume occupied by the gas; a study of the mechanical properties of a vacuum; and the first description of the effects of a low barometric pressure on a living organism (7, 9, 14). He wrote, ". . . what I once observed in a Viper, furiously tortured in our Exhausted Receiver, namely, that it had manifestly a conspicuous Bubble moving to and fro in the waterish humor of one of its eyes." Since he did not record the pressure to which the viper was exposed, one can only speculate as to the probable gaseous composition of the bubble in the aqueous humor.

During the eighteenth century Van Musschenbroek (7, 36, 50) reported the formation of bubbles in animals exposed to low pressures. In 1755 he wrote:

> We shut a rabbit in a glass receiver, and by means of a pneumatic pump drew out all the air; the animal at first was uneasy, sought air, swelled up all over; its eyes protruded . . . and finally died. The whole body of the animal swells in the vacuum because the ventricle [stomach] and the intestines contain much air . . . and distends the abdomen. But the blood and the other humors have elastic air mingled with their parts, which then, not being compressed, expands, recovers its elasticity, and distends all the vessels so that all the body of the animal must swell in all parts.

This is the first clear description of the swelling of an entire animal exposed to a vacuum and represents man's first observation of what may be tissue fluid vaporization. Traditionally, credit has gone to Hoppe-Seyler, who observed the same phenomenon one century later.

Hoppe-Seyler (35, 36) in 1857 placed frogs in a chamber which he then evacuated. His lucid description reads:

> As evacuation is continued, their bodies swell considerably due to expansion of the developing water vapor; water vapor escapes in bubbles through the mouth and the anus.

Two decades later Bert (7) conducted an extensive series of tests exposing various species of animals to variations in barometric pressure. He concluded that bubbles do not form in animals taken directly from normal to reduced barometric pressures. He did record one experiment which may represent his only observation of tissue liquid vaporization: In experiment 227 (on 10 March), he exposed a

320-gm. guinea pig to greatly reduced pressures for nearly 4 hours. Two hours and 50 minutes after beginning the exposure, he recorded:

> . . .5h 40m; pression 15c; ramene a 11c, 7; l'animal ne bouge pas, mais se gonfle manifestement . . .

He repressurized the animal to ambient pressure and left the laboratory that night. The guinea pig died during the night. The autopsy the following morning did not reveal bubbles in vessels. Perhaps an autopsy immediately following repressurization would have demonstrated the presence of gas.

Hill and Greenwood (30) in 1909 confirmed Hoppe-Seyler's findings of gas bubbles in vessels. They reported:

> A rabbit was decompressed in three minutes to 50 mm. Hg, at which pressure it died. The body swelled enormously during rarefaction. Post Mortem; the heart was found to be full of air[1] and all the large vessels contained numerous air bubbles. On the other hand, no bubbles were seen in eight mice, two guinea pigs, a cat and a kitten treated in the same way.

Armstrong (2, 4) in 1936 noted swelling in rabbit tissues, as had Van Musschenbroek in 1755. Armstrong constructed a glass chamber and was the first to observe the onset of bubbles forming in the blood of living animals at 58,000 feet barometric equivalent. Earlier, Boyle (7, 9) had described the boiling of warm lamb or sheep blood in vitro. Armstrong (2, 3) was the first to analyze the gaseous composition of the bubbles in the blood stream. Using a remote control blood sampling device, he sampled the blood of a goat after a 4-minute climb to 50,000 feet simulated altitude. He discovered:

In jugular vein			*In right ventricle*		
O_2	—	6.7%	O_2	—	11.4%
CO_2	—	28.3%	CO_2	—	28.3%
N_2	—	65.0%	N_2	—	60.3%
Total		100.0%	**Total**		100.0%

[1]Since they did not report a gas analysis, it is assumed that they meant gas instead of air.

X-ray demonstration of evolved gas resulting from decompression of a human from 5 atmospheres to 1 atmosphere was first reported by Gordon and Heacock in 1940 (21). The first x-rays of evolved gas occurring in human subjects exposed to lower-than-normal atmospheric pressures were reported by Thomas and Williams (61) in 1944. Their findings were:

> In every person with "bends" pain or with no "bends" pain, gas can be shown in the knee joint at an altitude of about 20,000 feet . . . The gas in the knee joint is not necessarily associated with pain, and may be freely aspirated. It consists of nitrogen, oxygen, and carbon dioxide, approximately in equilibrium with the normal blood gases.

Harvey et al. (25, 26) and Blinks et al. (8) demonstrated that muscular exercise and dissolved nitrogen and carbon dioxide are important variables partly responsible for bubble formation in animals exposed to a low pressure.

The first reported case of a swelling of the human hand at a low barometric pressure was recorded by Henry et al. (27) on 16 November 1944. The subject dressed in an early, experimental model of the partial-pressure suit and was denitrogenated for 1 hour. At ground level, he heated his hand in water at 48° C. for 5 minutes and then had a blood sample drawn from the back of one hand (29). He was then subjected to a chamber pressure of 59.6 mm. Hg. The unexpected results were as follows:

> After nine minutes at 58,000 feet during which time the subject had been alternately sitting and standing, moving his limbs to demonstrate their freedom and writing notes, the observers and the subject both noticed that his hands seemed larger than normal. The right hand in particular was swelling at an alarming rate. A puffiness of the dorsum appeared in a matter of seconds and painlessly increased until the hand was almost twice its normal size. It was deemed unwise to prolong the stay at altitude further and after 9½ minutes, at 58,000 feet, approximately 20 seconds after the swelling had first been noted, rapid descent was commenced and 40,000 feet attained in less than 15 seconds. During this descent the hand returned

to complete normality in spite of the maintenance of 85 cms. mask-vest pressure. At no time was there any abnormal subjective sensation and at no time throughout the run did the subject experience any "bends," "chokes," or gas pains.

Henry attributed the gaseous swelling to the vaporization of water vapor in the hand, which might have been precipitated by a nucleus of a nitrogen bubble.

In 1946 Henry et al. (28) performed experiments on 3 rabbits and 3 cats, each dressed in a pressure vest and exposed to 42 mm. Hg chamber pressure for 30 minutes. (These animals were not denitrogenated.) The gaseous swelling which uniformly developed at 42 mm. Hg was no longer visible at 140 mm. Hg chamber pressure.

Rascher (55) in May 1942 observed that human test subjects could survive brief exposure to a chamber pressure of 35 mm. Hg (21 km.) and that their blood did not boil at this low pressure. Hornberger (36) did not observe gas in the skin of his hand or elsewhere after a 10-second exposure to 48 mm. Hg (19 km.). Schubert and Grüner (58) and Kilches (44, 45) conducted studies on the formation of gas bubbles in animals rapidly decompressed to low barometric pressures. Kilches reported that the "degasification" of the blood begins at 77 mm. Hg (16 km.).

Jacobs (37) reported the occurrence of gas in the exposed right ankle of a subject exposed to 12.9 mm. Hg (27.4 km.) while wearing a USAF T-1 partial-pressure suit. The gas had disappeared by the time the chamber was at 68.8 mm. Hg (16.8 km.) and there were no aftereffects.

A tremendous amount of research was conducted at Ohio State University under contract with the National Research Council and later with the United States Air Force (33). Hitchcock et al. (31-34) reported on the response of the respiratory and gastrointestinal tracts and the circulatory and central nervous systems of dogs which were exposed to 30 mm. Hg pressure (22 km.). They used electrocardiograms, electroencephalograms, radiocontrast media, roentgenographic technics, cardiac and rib cage transparent Lucite windows, and open abdominal and visceral wounds to study the tissue responses. Vail et al. (62, 63) were the first to report their x-ray findings on the vaporization of tissue fluids. Edelman (15, 16) was the first to demonstrate that animal temperature may influence vaporization in the tissues. Two frogs were exposed to 30 mm. Hg. Body temperatures of the frogs were 20° and 29° C., respectively. The warmer frog swelled enormously, whereas the cooler frog did not. Kemph et al. (39-43) were the first to record the subcutaneous pressure which developed at 25 to 30 mm. Hg, and the first to record volume changes in animals during decompression and subsequent recompression. These investigators used the displacement of glycerin, ethylene glycol, saturated salt solutions, and mineral oils in measuring the changing volume of the animals (43). They also analyzed the gases in the gas pockets of dogs at 30 mm. Hg; these animals were not denitrogenated. They reported "high concentrations of water vapor and trace amounts of carbon dioxide" (40).

Strughold (60), in 1952, described the effects of animal exposure to low chamber pressures.

Wood (72-75) recorded some very interesting observations about subjects who were wearing the S-4 pressure suit. His subjects breathed 100 percent oxygen for 5 hours before the test. He noted the development of painless crepitation on the exposed hands after 2 hours of continuous exposure to 87 mm. Hg (15.2 km.) pressure. The crepitation disappeared at 100 mm. Hg (14.3 km.). Wood noted slight palmar crepitation after 1 hour at 68.8 mm. Hg (16.8 km.) even when snugly fitting gloves were worn (73). He did not take x-rays or analyze the gas in the hand (75).

Randel et al. (53, 54) did not report gaseous swelling of the exposed hands in a large series of subjects who were exposed to 68.8 or 42 mm. Hg chamber pressure for 1 minute.

Beischer and Born (6) used the Torricelli vacuum to study the effects produced by low pressures on various animals. They confirmed Bert's observations that animals with an exoskeleton usually do not die at very low pressures.

Ward (64) presented an excellent review of some aspects of the physical chemistry and physiology involved in gas formation in tissues exposed to low pressures.

McGuire et al. (48) published the first x-rays of a human hand exposed to 16 mm. Hg pressure (25.9 km.). His subject was denitrogenated for 2 hours. No gas analysis was performed (49).

Greider and Santa Maria (22, 56) studied the formation of a gas cavity in rats exposed to 20.8 mm. Hg chamber pressure (24.4 km.). They ingeniously employed a mixture of Dry Ice and isopentane at $-105°$ C. for quick freezing at low pressures. They then sectioned their rats with a fine band saw and recorded the occurrence of cavities in the frozen sections. They did not analyze the gas which formed (57).

While the Russians are aware of the effects of exposure of tissues to low pressures (51), they have not reported the results of any original work to date.

Wilson (70, 71) and White and Wilson (65) have also reported on the formation of enormous painless swelling in the hands of subjects dressed in pressure suits and exposed to low pressures. The hands of the denitrogenated subjects were exposed to chamber pressures between 3 and 20 mm. Hg. Visible swelling did not occur in one subject whose hand was exposed to 8 mm. Hg chamber pressure for 20 minutes (71).

Kittinger (46) and Chubb (13) reported an accidental failure of a right pressure glove with the subsequent formation of swelling and crepitation during an open gondola ascent to 31.3 km. (The subject had been denitrogenated for $2\frac{1}{2}$ hours before ascent.) Chubb and one other physician noted that "there was marked swelling and some crepitus . . . shortly after landing. [The crepitus disappeared in about 20 minutes.] The blood pressures recorded about 45 minutes after landing were: RA 160/110; LA 130/80; LL 160/110; RL 160/110. The discrepancy in arm blood pressures was gone the next day and could conceivably have been due to autonomic vasoconstriction in the right arm from the dysbarism."

Since Boyle's first observation of a gas bubble in the viper's anterior chamber, investigators have studied the effects of bubble formation in various animals with various body temperatures at various low pressures for various periods of time under a variety of states of denitrogenation. The present investigator desired to accomplish some studies on the human hand while attempting to control the seemingly more important variables of denitrogenation, temperature, muscular activity, blood flow, chamber pressure, and time.

METHOD OF INVESTIGATION

The main objective of this research was to measure quantitatively the onset and disappearance of swelling in the hand while subjecting it to various total pressures. No device was known to exist which would measure this change in volume. The investigator chose three distinct methods with the hope that one or more of them might prove to be suitable. The methods were: displacement of a suitable fluid in a plethysmograph; roentgenography; visual observation.

Development of plethysmograph

The main problems were:

1. To develop a rugged, rigid, transparent, small, inexpensive plethysmograph suitable for measuring the changing volume of the human hand.

2. To devise a simple and effective means of sealing the wrist of the subject where the arm enters the box, yet to allow the subject to quickly withdraw his hand if an emergency should arise.

3. To provide for the rapid escape of gas bubbles which may evolve from the fluid in the plethysmograph.

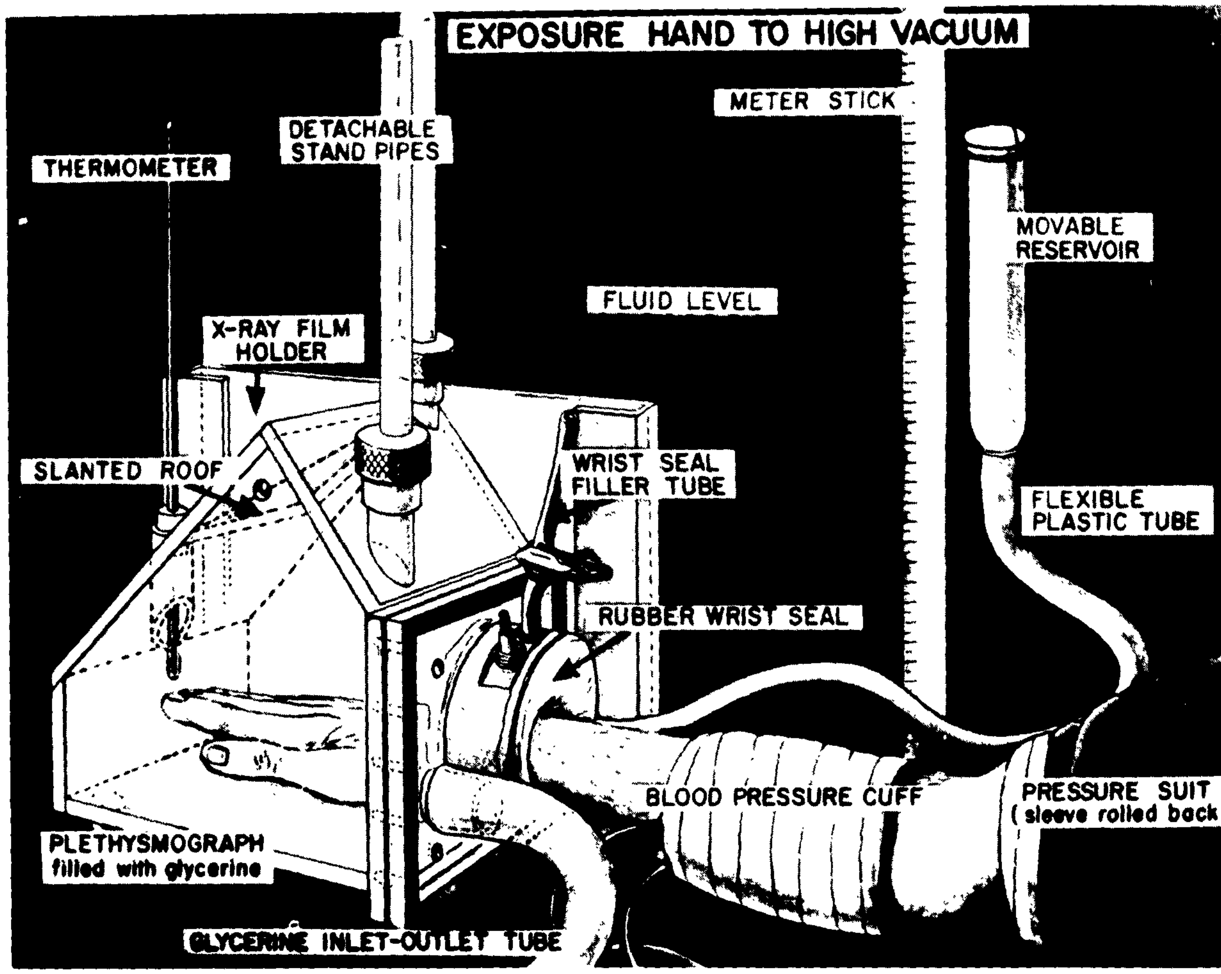

FIGURE 1

Hand plethysmograph.

4. To provide for a rapid direct reading of the change in volume of the hand in the box.

5. To provide for control and measurement of the temperature of the fluid.

6. To provide the means for rapid filling and emptying of the plethysmograph at any chamber pressure, including 3 mm. Hg (36.6 km.).

7. To provide the means for maintaining a constant hydrostatic pressure on the hand during the experiment, as the fluid is displaced.

8. To provide for easy cleaning and repair of the box and of the wrist seal.

A plethysmograph was developed which met the requirements outlined above (fig. 1). The floor, walls, and slanted roof were constructed of Plexiglas 9 mm. thick. The inside dimensions were: width, 16.7 cm.; depth, 20 cm.; height in front, 12 cm.; greatest height, 20.0 cm.; height at back, 7.3 cm.

A slanted inside roof was later inserted (fig. 1) and positioned so that all bubbles in the plethysmograph would rise and escape through the uppermost standpipe. A hole, 1 cm. in diameter, was drilled in the wall of the box above the slanted roof to allow unrestricted ingress and egress of air during chamber operation. Two standpipes of Plexiglas tubing were affixed to the box. The pipe on the lower part of the front roof had an

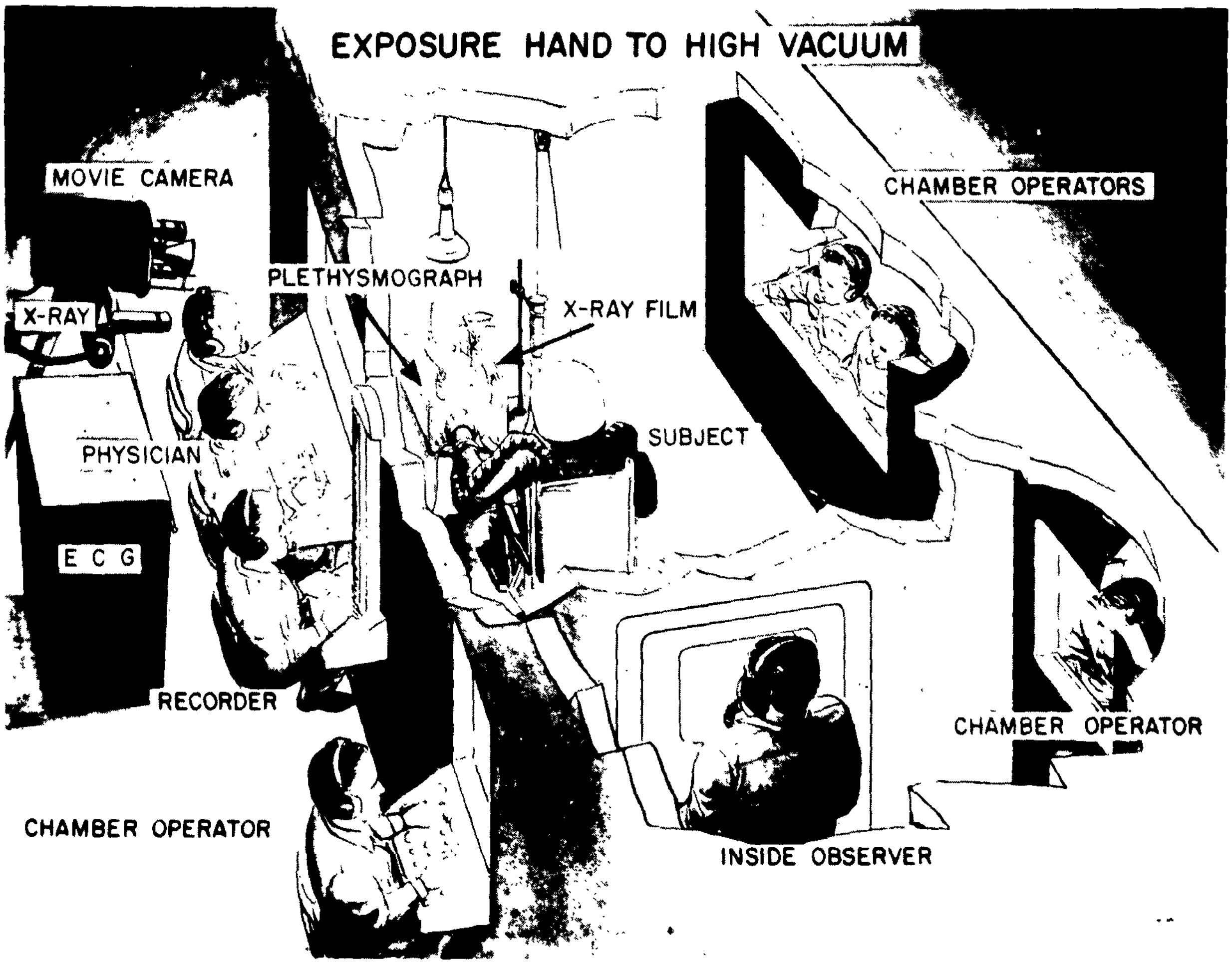

FIGURE 2

Research team monitoring the experiment.

internal diameter of 2.2 cm. The pipe at the top of the roof had an internal diameter of 1.5 cm. Each pipe (28.5 cm. long) was calibrated; it was detachable to avoid breakage while the box was being carried, cleaned, or stored. The back roof of the box was fitted with a simple pipe (I.D., 2.2 cm.), which housed a removable mercury thermometer held in position by a rubber stopper. To avoid the trapping of air in this thermometer pipe, the rubber stopper was inserted in the bottom of the pipe (not as shown in figure 1).

A removable plate at the front of the box contained two rigid plastic tubes (I.D., 1.2 cm.; O.D., 1.9 cm.). The tubes (2.8 cm. long) were positioned on each side of the wrist-seal device. These rigid male tubes were fitted to flexible, translucent plastic tubing (I.D., 1.9 cm.). This flexible plastic tubing (1 m. in length) was connected to a movable, calibrated glass reservoir (volume, about 250 cc.). The glass reservoir could be raised or lowered by a nylon cord placed over a pulley attached to the ceiling (fig. 2). Another length (2 m.) of flexible plastic tubing (the glycerin inlet-outlet tube in figure 1) was attached to a 5-gallon drum. The drum had been fitted with a soldered brass spout at the base to allow liquid to flow out when the drum was raised and to flow in when it was lowered. An aluminum stopcock (1.9 cm. in diameter) was interposed along the course of the longer section of tubing to permit control of the direction of flow of the liquid.

The wrist-seal device (fig. 1) consisted, in part, of a rigid hollow cylinder attached to the removable front plate. The rigid cylinder was formed by laminating five plates of Plexiglas and cutting a large hole out of the solid piece. The laminated cylinder had an internal diameter of 8.8 cm. and an outside diameter of 10.9 cm. It extended 4.3 cm. in front of and 1.4 cm. behind the removable plate. A brass wrist-seal filler tube was permanently mounted on the top of the laminated cylinder (fig. 1). Bubbles could then be easily removed from the rubber wrist-seal bag when it was filled with fluid. The wrist portion of latex surgical gloves, size 8, provided a durable seal. The rubber was stretched over the outer and inner ends of the laminated cylinder and was tied to the laminated cylinder to prevent any leakage of fluid. A circular groove was cut near both ends of the laminated cylinder to facilitate a tight and secure fit of the latex with the plastic. The removable plastic front plate was joined to the rest of the plethysmograph by screws. A neoprene gasket was interposed between the removable plate and the box to prevent leakage. Filled with fluid to a level just above the point where the standpipes detach, the box has a volume of 5,200 ml.

Choosing a fluid

The following characteristics were desired for the fluid:

1. It should be nontoxic, incompressible, inexpensive, and transparent to both the visible and the x-ray wavelengths of the electromagnetic spectrum.

2. When heated to 45° C. it should not boil at a chamber pressure of 3 mm. Hg (36.6 km.).

3. It should have a low specific gravity so that it would not offer much hydrostatic counterpressurization to the hand.

4. Its specific gravity should not change greatly over a temperature range of 30° to 45° C.

5. It should have a low viscosity in the temperature range of 30° to 45° C.

Gas could not be used as the fluid because it did not satisfy all the conditions listed above. Solids also were discounted as not suitable. Among the liquids available, several boil only when subjected to extremely low pressure and high temperature (38). Glycerin was chosen because it is nontoxic (19, 20, 24, 59) and boils only when heated to 125° C. and exposed to a pressure of 1 mm. Hg (38). Only later, it was discovered to be radio-opaque to the 80 kv. x-rays and thus did not fulfill all requirements.

Roentgenographic technic

X-ray photographs were desired under the following conditions:

1. Exposure of the human subject to x-rays was always to be kept to a minimum while achieving the necessary records during the test.

2. All personnel were to be closely monitored for accidental or excessive experimental exposure to ionizing radiation.

3. A portable x-ray unit would remain outside of the chamber (fig. 2) to prevent rupture of the insulation and damage to the expensive equipment. There would be a constant distance of 102 cm. between the x-ray tube and the photographic film.

4. X-rays would be directed at the chamber wall, through an aluminum port 3.18 mm. thick and 17.8 cm. in diameter. In earlier tests x-rays were successfully directed through the standard glass of the window of the altitude chamber so as to produce films of fair quality. If there is no chamber port for x-rays this can be accomplished using 80 to 90 kv. for 100 mas. (milliampereseconds). X-ray films of the hand would be taken while the hand was in the glycerin-filled box. Later, .. rays were taken with the hand out of the box, however.

5. The x-ray technic would be so adjusted as to provide the finest possible details of the soft-tissue structures of the hand. To accomplish this, a cardboard film holder was used.

6. The x-rays would be properly identified as to subject and experimental condition.

7. Selected developed x-rays would be processed by a Logotronic machine to enhance the contrast in soft tissues.

Photographic technic

Motion picture (16 mm.) color strips were taken during moments of apparent hand swelling on each test. The floodlights were installed in the chamber and operated by remote control by the camera crew outside the chamber (fig. 2). A capstan pressure gage was converted into an accurate movie altimeter by placing a properly labeled disc over the numbers showing pounds per square inch. Hence O equaled 40,000 ft., and 14 p.s.i. equaled 120,000 ft.

Subjects

Before the test, the investigator carefully reviewed all medical records, EKGs, x-rays, and laboratory data on each subject to be sure that he was medically acceptable as a test subject. The subject was physically examined 6 hours before the test. At 1230 hours on the day of test, the subject began 2 hours of denitrogenation while breathing 100 percent aviator's oxygen. Each subject began denitrogenating while wearing an A-13-A oxygen mask and later switched over to the MA-2 full head helmet while holding his breath. This arrangement was more comfortable than that of requiring the subject to wear the MA-2 helmet for the 2 hours. Before the subject was completely dressed in the pressure suit, the investigator examined his ears with an otoscope. The otoscopic examination was easily accomplished while the subject held the A-13-A mask to his face. Three indirect blood pressure readings from each arm were also recorded while the subject sat. During denitrogenation the subject was dressed in his previously fitted partial-pressure suit (type MC-3 or MC-3A). The only modification of the routine fitting of the pressure suit was to loosen the sizing laces of the entire left forearm and to roll the left sleeve of the pressure suit back to the elbow. The sleeve was snugly fitted at the elbow by Ace bandage or masking tape (fig. 3). This arrangement provided adequate counterpressurization to the upper arm but left the remainder of the arm exposed from about the elbow distally as was desired. A pneumatic cuff was secured to the forearm, without being tight enough to cause venous distension. Suitable inflation of the pneumatic cuff enabled the investigator to stop the flow of blood into and out of the hand distal to the cuff (figs. 1 and 3). Electrocardiographic leads were placed on the limbs of each subject. Regulation flying boots were worn. To avoid leaking of the faceplate exhalation valve at very low chamber pressures (68), a circular band of No. 60 mesh brass screen was closely fitted over each exhalation valve. Toward the end of the denitrogenation period, the subject walked to the chamber, still breathing 100 percent oxygen from a walk-around bottle. He was seated in a modified ejection seat and the following preparations were carried out:

1. The pressure suit helmet, bladder, and capstan tubes were connected to the seat kit regulator.

2. The press-to-test button was pushed in order to check the delivery of adequate pressures from the seat kit regulator to the suit.

3. The chamber air-conditioning was turned on for the comfort of the subject.

4. The helmet intercommunication was connected and checked with all chamber stations.

5. The electrocardiographic leads were attached to a cable which penetrated a tap on the chamber wall. Air leakage through the wall was prevented by the use of a rubber stopper and clay. A technician adjusted the oscillograph and direct write-out so that the tracing could be read and permanently recorded by the investigator (see fig. 2).

6. The pneumatic cuff on the forearm was attached to two Tygon plastic tubes (No. 1080). One tube originated outside of the chamber wall. This tube had a simple screw-type metal valve which allowed room air to flow into the tube when the valve was turned on. The tube penetrated the chamber wall and was directly attached to the pneumatic cuff. The second plastic tube originated at the pneumatic cuff and went directly to a Tycos aneroid manometer. Pressure manometers such as the familiar blood pressure manometer are most easily interpreted when the manometer is exposed to the same ambient pressure as the subject. This becomes a problem in pressure suit research since there is little room in the suit for the manometer. This deficiency was solved by building a leakproof plastic box capable of holding an internal pressure of 150 mm. Hg in excess of external pressure (fig. 4). Suit bladder pressure was delivered to the

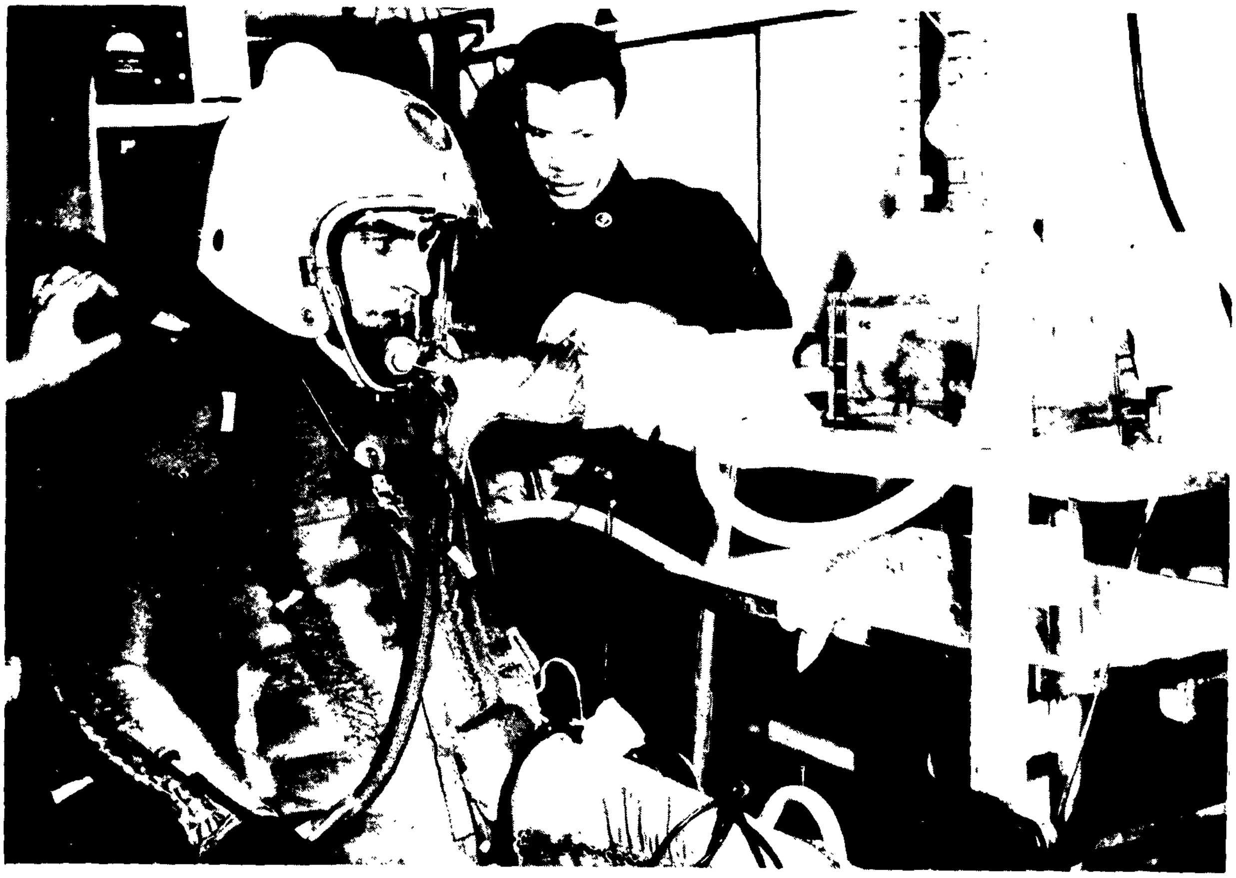

FIGURE 3

Preparing the subject for the experiment.

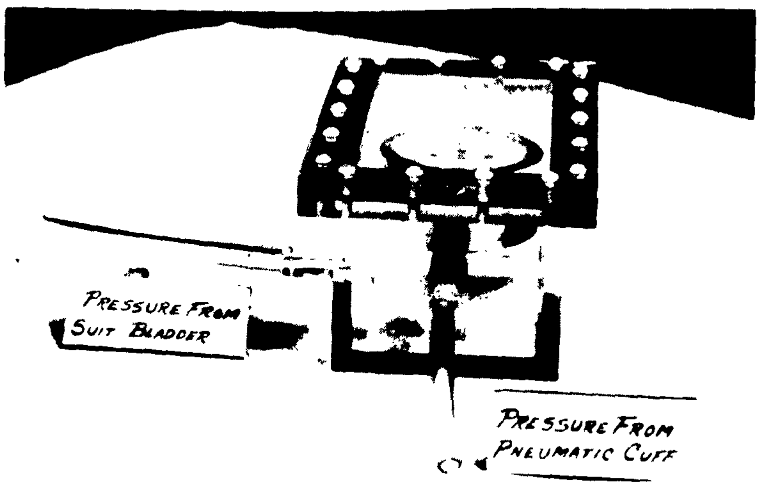

FIGURE 4

Pneumatic cuff manometer mounted in a pressure box.

plastic box containing the manometer by tapping off pressure from the bladder hose. The Tycos manometer was permanently mounted in the plastic box with its pressure-sensing line penetrating the floor of the box.

7. The subject's hand was lubricated with glycerin and inserted through the rubber wrist seal of the plethysmograph. The rubber wrist seal, filled with approximately 250 cc. of glycerin, was very comfortable. Care was taken to remove all bubbles from it. The bubbles could easily be seen through the translucent rubber. A folded towel was placed under the subject's elbow to enhance comfort. The 5-gallon can of prewarmed glycerin was raised above the plethysmograph; the aluminum valve was opened, allowing glycerin to flow into the plethysmograph. The box was filled up to the first calibration mark on the standpipe next to the meter stick (figs. 1 and 3).

8. For further warming of the glycerin, a 200-watt spotlight was placed over the plethysmograph.

9. The distance between the center of the hand and the top of the glycerin was measured so that the hydrostatic pressure exerted by the glycerin on the hand could be computed.

10. A final check was made of the helmet, brass screen modification, helmet cable, helmet tiedown ribbon, and suit pressures on a press-to-test.

Test profile

Each subject was tested for 5 minutes at a low chamber pressure. If a swelling of the hand did not occur, the chamber pressure was returned to 206 mm. Hg (9.8 km.); the aluminum valve was opened to allow the glycerin to flow back into the 5-gallon drum, and the hand was withdrawn from the rubber wrist seal. The glycerin was left in the wrist seal. The plethysmograph was moved aside and a lead box containing photographic film in cardboard holders was placed within easy reach of the subject. The chamber was then evacuated to approximately 3 mm. Hg chamber pressure (36.6 km.), and the hand was observed for swelling. A record was made of the duration of time between reaching the low chamber pressure and the development of visible swelling of the hand. When swelling was observed, the subject immediately placed his hand against the preplaced film, and an x-ray exposure was made. The chamber then was immediately repressurized to higher pressures and additional x-ray exposures were made. The time from the onset of swelling to the exposure of the last film never exceeded 3½ minutes.

The hand of the subject was replaced in the plethysmograph at 206 mm. Hg (9.8 km.) and the box refilled with glycerin. When volumetric increases were recorded, the chamber was repressurized in a stepwise fashion to verify the volumetric displacement. When this was completed, the chamber experiment was terminated. Every subject opened his faceplate at 522 mm. Hg chamber pressure in an attempt to reduce the incidence of delayed aerotitis media.

Test followup

Immediately after the test the following were recorded:

1. The general appearance of the subject.
2. The presence or absence of crepitation on the forearm and hand by palpation and auscultation.
3. The appearance of the ear drums and middle ears.
4. The blood pressure in both arms by the technic described earlier.

The subject was instructed to rest for the remainder of the day, to contact the investigator by telephone if he began to develop any signs or symptoms of dysbarism, and to see the investigator the next morning.

On the following morning, data were recorded as to—

1. General appearance of the subject.
2. Examination of ears and questioning about ear pain during sleep or upon awakening.
3. Blood pressure in both arms by the technic described above.
4. Examination of the hand.

Each subject's hand was examined three months later to establish the presence or absence of any apparent injury or sequela.

FIGURE 5

X-ray of hand after 5 minutes' exposure to 5 mm. Hg chamber pressure (33.5 km.).

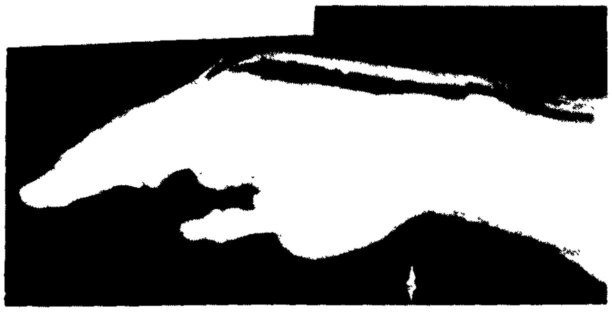

FIGURE 6

X-ray of hand after 7 minutes' exposure to 5 mm. Hg chamber pressure (33.5 km.).

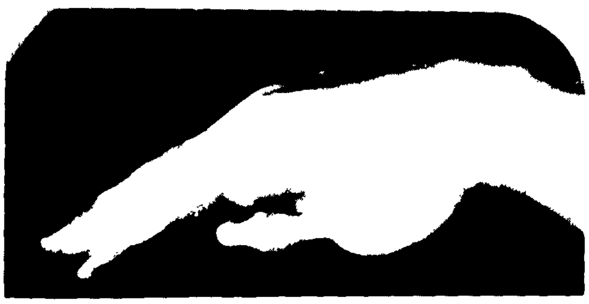

FIGURE 7

Hand repressurized to 87 mm. Hg chamber pressure (15.4 km.) after 9 minutes at 6 mm. Hg (34 km.).

FIGURE 8

X-ray hand at 141 mm. Hg chamber pressure (12.2 km.) after 11 minutes' exposure to 3 mm. Hg (36.6 km.).

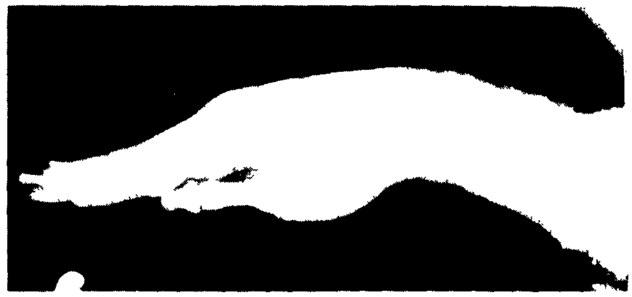

FIGURE 9

X-ray hand repressurized to 206 mm. Hg chamber pressure (9.7 km.) after 2 minutes' exposure to 5 mm. Hg (33.5 km.).

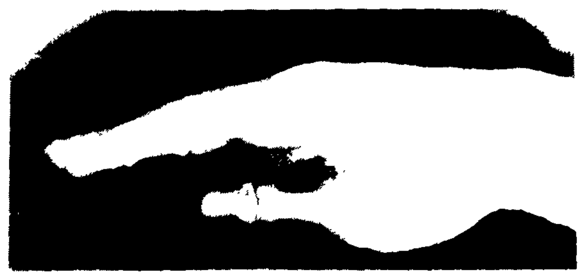

FIGURE 10

X-ray hand at 226 mm. Hg chamber pressure (9.1 km.) after 11 minutes' exposure to 3 mm. Hg (36.6 km.).

Criteria for determining gaseous swelling

When the hand was immersed in glycerin, gaseous swelling was recorded as having occurred only if there was a simultaneous visible swelling and measurable increase in the volume of the ischemic hand.

Whenever the hand was exposed to the air pressure alone, gaseous swelling was recorded as having occurred and subsided only when unequivocally demonstrated on x-ray film. In those cases where there was a question of continued presence of gas in the tissues, the final interpretation rested with a specialist in roentgenographic technics and interpretation.

A special measurement was devised for use on those lateral x-ray films of the hand where gas was demonstrated. To express the amount of swelling in a semiquantitative fashion, two measurements were made and a ratio computed. The measurements were made in the following manner:

1. Only lateral films of the hand were used.

2. The metacarpal bone shadow, which was most dorsally situated, was selected in each series of films (figs. 6 to 12).

3. A point *A* was placed on the film on the dorsal edge of that metacarpal bone, equidistant from the two ends of the bone.

4. A line was drawn through point *A*, perpendicular to the long axis of the metacarpal bone and up toward the dorsal surface of the skin shadow.

5. The intersection of the line perpendicular to point *A* and the dorsal surface of the skin shadow was called point *B*.

6. The distance between points *A* and *B* was measured on all x-ray films in a series showing the presence of gas under the skin on the back of the hand.

7. A ratio was computed. The numerator contained the distance in millimeters between *A* and *B* when gas was present. The denominator contained the distance between *A* and *B* of the same hand exposed to atmospheric pressure.

8. A ratio of greater than 1.0 signifies that there was gaseous swelling under the skin. This ratio was termed the *skin elevation ratio.*

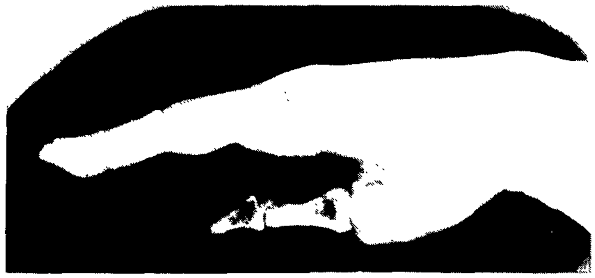

FIGURE 11

X-ray hand at 349 mm. Hg chamber pressure (6.1 km.) after 11 minutes' exposure to 3 mm. Hg (36.6 km.).

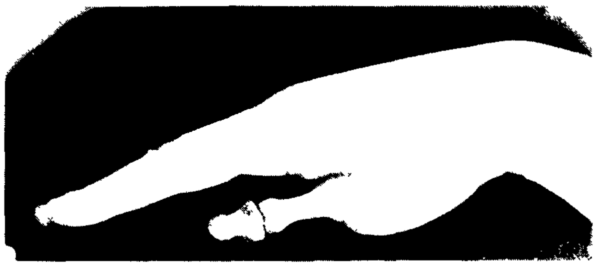

FIGURE 12

X-ray hand at 750 mm. Hg chamber pressure (0.0 km.) after 11 minutes' exposure to 3 mm. Hg (36.6 km.).

FINDINGS

Six different subjects were tested. One subject was tested five times and 5 other subjects were tested one time each. See table I.

The first six experiments were devoted mainly to the development of a suitable plethysmograph and to the modification of roentgenographic technics. An unsuccessful series of attempts was made to penetrate the 166-mm. thickness of glycerin in the plethysmograph. In a final attempt, the x-ray film was exposed to rays which came from a portable machine set to deliver 100 kv. rays for 200 mas. This maximum setting produced a very faint outline of the bones of the hand, but soft-tissue contrasts were absent. No further attempts were made to take x-rays while the hand was in the glycerin-filled box mainly because overheating of the x-ray tube's

TABLE I

Log of all tests on experimental subjects

Expt. No.	Subject	Date	Number of x-ray films taken	Was gas demonstrated by x-ray?	Remarks
1	CW	21 Nov. 60	5	No	Ulnar paralysis developed during test owing to constant pressure of an experimental adjustable plastic plate around wrist. Normal function immediately returned on removal of hand from box.
2	RH	30 Nov. 60	5	No	Unable to obtain good soft-tissue definition when using x-ray with hand in glycerin, even when using 100 kv. x-rays for 200 mas.
3	CW	12 Dec. 60	8	No	Took x-ray film exposures of wrist outside of the plethysmograph. Directed x-ray beam through the chamber window using 86-100 kv. for 200 mas. Obtained good soft-tissue details of wrist.
4	CW	10 Jan. 61	2	No	Removed glycerin from plethysmograph using rapid dump valve. Good soft-tissue definition demonstrated using an x-ray beam penetrating both the chamber glass and the empty plastic box.
5	GL	11 Jan. 61	0	No	Since previous x-ray technic modifications have not shown gas but do show good soft-tissue definition, will not take further x-rays until able to secure suitable chamber with x-ray port.
6	CW	26 Jan. 61	4	Yes	X-rays demonstrate definite gas in wrist joint, x-rays directed through aluminum port 3.2 mm. thick. Test aborted immediately after x-rays taken, owing to loss of intercommunication and ECG.
7	CS	2 Feb. 61	6	Yes	Excellent quality x-rays, using 38 kv. and 100 mas. All subsequent x-rays directed through the aluminum port 3.2 mm. thick.
8	SK	8 Feb. 61	5	Yes	Excellent quality x-rays using 42 kv. and 100 mas. Hand swelled on second exposure in glycerin at low pressures.
9	CW	15 Feb. 61	6	Yes	Excellent quality x-rays using 42 kv. and 100 mas. Hand swelled on second exposure in glycerin at low pressures.
10	JM	8 Mar. 61	7	Yes	Excellent quality x-rays using 38 kv. and 100 mas. Hand swelled on second exposure in glycerin at low pressures.

TABLE II

Development of gas in the hand: First exposure of hand to low total pressures with the hand in the glycerin-filled plethysmograph

Expt. No.	Did visible hand swelling occur?	Increase in volume of hand (cc.)	Lowest total pressure on hand (mm. Hg)	Time of exposure to lowest total pressure (min.)	Temperature of glycerin (°C.)
1	No	0	49.0	1.5	31.0
2	No	0	35.0	2.5	28.0
3	No	0	40.4	5.0	35.0
4	No	0	38.2	5.0	35.0
5	No	0	36.0	5.0	36.0
6	—	—	—	—	—
7	No	0	20.7	2.0	42.5
8	No	0	16.2	5.0	39.5
9	No	0	25.0	5.0	40.0
10	No	0	19.7	5.0	35.0

target might permanently damage the tube. While decreasing the width of the plethysmograph might have ultimately produced soft-tissue x-ray films of good quality, redesign of the box would have been so expensive and time-consuming as to delay completion of the project.

Satisfactory x-ray pictures of the soft tissues of the hand were ultimately taken through an aluminum port of 3.2 mm. thickness at an x-ray machine setting of 38 to 42 kv. and 100 mas. See table I. The exposure was 10 seconds at 10 ma. in experiments 7 through 10. Table I shows, also, that when the once-swollen hand was again placed in the glycerin-filled plethysmograph, a measurable increase in the volume of the hand did occur at greatly reduced chamber pressures.

Each subject's hand was exposed to a variety of low total pressures. Table II records the results of the first exposure in glycerin. Since it was not possible to take the x-ray pictures in this part of the experiment, only the presence or absence of visible swelling and the volumetric change were recorded. In no case was the hand observed to swell the first time it was exposed in glycerin. No measurable increase in the volume of the hand occurred during the first exposure. The total pressure (as referred to in table II) is the sum of all of the pressures exerted on the hand of the subject: air pressure of the chamber and hydrostatic pressure of the glycerin.

Example: Chamber pressure, 7.0 mm. Hg. Height of glycerin column above hand, 152 mm.

$$\text{Hydrostatic column (mm. Hg)} = \frac{(152 \text{ mm. glycerin})\ (1.26 \text{ sp. gr. glycerin})}{13.6 \text{ sp. gr. Hg}}$$

Hydrostatic column = 14.1 mm. Hg

Total pressure = 7.0 + 14.1

Total pressure = 21.1 mm. Hg

Table III records the events which occurred when the hand was removed from the plethysmograph and exposed only to the low pressure of the chamber. Experiments 3 and 4 showed that definite visible and photographic swelling of the hand could occur without the demonstration of gas by x-ray. The x-ray technic is much more sensitive than the visual method of determining the disappearance of

TABLE III

Development of gas in the hand: Second exposure of hand to low chamber pressure with hand removed from glycerin-filled plethysmograph

Expt. No.	Did x-ray films demonstrate gas in hand?	Did hand appear swollen visibly?	Lowest pressure to which hand was exposed (mm. Hg).	Length of time at lowest pressure before gas developed or until test was discontinued (min.).	Highest pressure at which the hand still had traces of gas or visible swelling, once swelling developed (mm. Hg).	
					By x-ray	Visually
1	—	—	—	—	—	—
2	No	No	10.2	5.0	—	—
3	No	Yes	6.0	3.0	—	87
4	No	Yes	10.0	2.0	—	87
5	—	Yes	8.0	1.0	—	111
6	Yes	Yes	25.2	1.0	25.2*	111
7	Yes	Yes	5.0	4.0	5.0*	128
8	Yes	Yes	5.0	7.5	140.7*	87
9	Yes	Yes	7.0	0.5	205.6*	111
10	Yes	Yes	5.0	10.3	225.6	140.7

*Additional x-rays were not taken at higher chamber pressures. Posttest x-rays at atmospheric pressure (750 mm. Hg) were normal.

TABLE IV

Skin elevation ratio

Expt. No.	Chamber pressures (mm. Hg)								
	5	87.3	110.9	140.7	178.7	205.6	225.6	349.1	750
7	2.7 2.8	—	—	—	—	—	—	—	1.0
8	4.4	2.1	1.8	1.6	—	—	—	—	1.0
9	3.6	—	1.6	1.4	1.2	Trace still visible, 1.0	—	—	1.0
10	3.0	1.8	—	1.2	—	—	1.1	1.0	1.0

gas, once it has developed. The hand of each subject in experiments 9 and 10 still showed definite traces of gas under the skin by x-ray examination at 205.6 and 225.6 mm. Hg chamber pressure, respectively. No gas was discernible by x-ray at 349.1 mm. Hg chamber pressure in the hand of subject 10. No gas could be demonstrated in the hand of any subject at 750 mm. Hg atmospheric pressure (figs. 5 to 12).

Table IV presents the findings when the skin elevation ratio was measured on the x-ray film. There was a progressive decrease in the

TABLE V

Development of gas in the hand: Third exposure of the hand to low total pressures with the hand replaced in the glycerin-filled plethysmograph

Expt. No.	Did visible swelling of the hand occur?	Volume of normal hand (ml.)	Increase in volume of hand (ml.) At total pressures (in mm. Hg) of—						Temperature of glycerin (° C.)
			190	150	100	90	70	50	
8	Yes	390	0	0	39	46	59	78	36.0
9	Yes	370	0	0	0	0	8	28	36.0
10	No	460	0	0	16	18	28	28	32.0

ratio with an increase in chamber pressure, and the results in each experiment were closely comparable at the various chamber pressures. In experiment 9 a trace of gas was seen on the film (fig. 9), but the skin elevation ratio was 1.0.

Table V records the change in the volume of the hand in the last three experimental subjects. After gaseous swelling of the hand in air was evoked, the hand of each of the last three subjects was replaced in the glycerin-filled plethysmograph. In each case a volumetrically measurable swelling did occur — measurable between 70 and 100 mm. Hg total pressure. In experiment 10 there was significant volumetric swelling of the hand but no visible swelling. In the other two experiments the swelling was both measurable and visible.

Table VI presents a condensation of medical data collected before, during, and after each experiment. The average of three blood pressure recordings demonstrates no significant difference between pretest and posttest pressures.

Miscellaneous observations

There was only one moderately severe case of delayed aerotitis media after 4 hours of denitrogenation and removal of the faceplate at 522 mm. Hg chamber pressure. Twenty hours posttest there was pain and bubbling in both ears when a gentle effort was made to equalize pressures around the tympanic membrane by the Valsalva maneuver. No symptoms of decompression sickness occurred among the subjects during or after the test.

The pulse climbed rapidly to rates of 100 to 140 during experimental exposure of the subject to extremely low barometric pressures. The pulse rates promptly returned to normal on chamber repressurization.

Subjective sensations on the development of gas in the hand were notable because of the absence of pain in all cases. The typical initial sensation was one of a sudden appreciation of the skin being stretched in a localized area on the back or palm of the hand, or at the wrist. Sometimes it felt as if ants were running over the skin. On other occasions it felt as though air was being injected under the skin. The swelling would progress over the back of the hand very rapidly, expanding the gas pocket and elevating the skin until it was tense and slightly shiny and the back of the hand was markedly convex. Even though the swelling was marked, the subject maintained the ability to flex and extend the wrist and the fingers through about a 50 percent range of motion. While the chamber was being repressurized to 141 mm. Hg pressure, the swelling usually seemed to disappear, normal range of motion was immediately normal again, and palpation of the hand with a gloved right hand did not reveal crepitus. Immediately upon reaching 750 mm. Hg atmospheric pressure the hand was examined. There was no instance in which the presence of gas could be demonstrated at normal atmospheric pressure by palpation, inspection, auscultation, or roentgenography.

TABLE VI

Medical data before, during, and after experiment

Expt. No.	B.P. (av. of 3 recordings)						Denitrogenation time before test (min.)	Delayed aerotitis media*	Total time at chamber pressure less than 225.6 mm. Hg (min.)	Dysbarism	Pulse average at 206 mm. Hg chamber pressure	Highest pulse rate during test
	Before test		Immediately after test		20 hours after test							
	R	L	R	L	R	L						
1	—	—	—	—	—	—	150	(1)	18	0	82	140
2	133/83	143/90	148/88	140/83	—	—	210	0	28	0	—	—
3	—	—	—	—	—	—	155	0	81	0	85	120
4	—	—	—	—	—	—	150	0	66	0	82	112
5	102/75	102/70	116/78	112/78	102/75	102/70	130	0	85	0	80	104
6	—	—	—	—	—	—	240	(2)	30	0	—	—
7	108/72	106/73	112/62	119/72	112/64	112/76	155	0	86	0	75	120
8	132/82	137/88	123/93	133/91	122/83	130/88	190	(3)	82	0	100	132
9	103/64	102/64	102/67	102/71	100/62	104/64	160	0	40	0	94	120
10	117/74	118/77	120/74	130/78	113/76	115/76	200	0	58	0	80	100

*Occurred in 3 subjects: (1) Awoke twice because of ear pain; relieved by Valsalva maneuver. (2) Moderately severe pain with decreased hearing acuity; bubbles; resolved in 48 hours. (3) Slight pain in both ears on arising—after Valsalva maneuver had caused bubbling in left ear.

Followup two months later indicated no injury or sequela.

DISCUSSION

There was no visible or measurable increase in the volume of the ischemic hand when it was immersed in the glycerin-filled plethysmograph and initially exposed to a very low total pressure for a brief period of time (table II). When the hydrostatic weight of the glycerin was removed, there was demonstrable gas in five out of nine experiments. Surprisingly, the gas did not disappear until chamber pressures much greater than predicted had been achieved. On subsequent exposure of the once-swollen hand to low pressures while immersed in the glycerin, the hand swelled at chamber pressures much greater than predicted.

It is reasonable to assume that any swelling which occurs in an ischemic hand exposed to a constant temperature and a very low total pressure cannot be due to an increase in the volume of liquid from transudation but must be due to the formation of a gas. This assumption is supported by the fact that the swelling is rapidly reversible and easily demonstrated by a suitable roentgenographic technic. The gas which develops must come from substances in the ischemic hand. Certain elements and compounds present in the human hand are known to exist in a gas phase at about 37° C. at very low total pressures; they are oxygen, nitrogen, carbon dioxide, argon, and water. Nitrogen and argon can be eliminated, for the most part, when one breathes 99.5 percent oxygen for 130 minutes or longer. It is assumed that no large gas pockets pre-existed in the hand to serve as nuclei for the initial exposure to low pressures. In this series of experiments, the reversible formation of gas most likely was caused by water, carbon dioxide, and oxygen. It is theoretically possible that tissue fluids containing a very high concentration of ethyl alcohol could appreciably alter the vapor pressure of water. Actual circumstances directed that this theoretic consideration was not a factor.

If the evolved gas were composed entirely of pure water molecules, then that gas would behave as any other simple physical system. At body temperature water will pass into a gas phase at low total pressures. Pure water molecules, in a liquid state and at a temperature of 32° C. or greater, will pass into a gaseous state whenever the total pressure is less than 35.7 mm. Hg (47). The temperature of 32° C. was arbitrarily chosen as the lowest surface temperature likely to be found on the hands of the subjects during the testing in air. In estimating the total pressure exerted on the liquid in the hand one must consider the elastic tension of the connective tissue, the static hydrostatic weight of the solid and liquid components of the tissues, and the hydrodynamic pressure caused by the systemic circulation. The inflated pneumatic cuff eliminates the hydrostatic force from the systemic circulation. The elastic tension and static weight of the tissue have been considered as unchanged, but of an undetermined magnitude.

As stated above, if water molecules in a liquid state at a temperature of 32° C. or greater were exposed to a total pressure of less than 35.7 mm. Hg, those molecules would undergo transition into a gas. Table II demonstrates that gas did not develop in any ischemic hand at pressures even as low as 16.2 mm. Hg with temperatures even as high as 39.5° C. Since water is present in the hand in great quantity, and since the vapor pressure of that water is increased only slightly (0.25 mm. Hg) by the presence of nonvolatile solutes (64), one must assume that the combined effect of the elastic tension of connective tissue and the weight of the tissue prevented the water from passing into a gaseous phase at such low pressures. Table III demonstrates that further lowering of the total pressure caused swelling of the hand but that it occasionally required 10 minutes to produce it. Once the swelling started, it progressed rapidly, apparently popping strands of connective tissue as it expanded.

In general, the hand swelled within a few minutes when the total pressure was less than 8 mm. Hg. If one assumed that the gas which first developed was nearly all water vapor, then he might reasonably conclude that a connective-tissue counterpressure had been temporarily effective in maintaining the water in a liquid state. That counterpressure would be roughly equal to the difference between the vapor pressure of water at 32° C. and the total pressure at which gas was first seen. Subtracting 8 mm. from 35.7 mm. Hg yields a rough estimate of 27.7 mm. Hg counterpressure provided by the connective tissue. If one assumes that CO_2 was exerting a tension of 40 mm. Hg or more, then the connective-tissue pressure necessary to prevent gas formation was more nearly 67.7 mm. Hg. The tension of CO_2 increases with time in the ischemic hand. Perhaps the combined tensions of CO_2 and H_2O play a role in the final formation of a bubble.

If the gas which developed were pure water vapor and the gas remained constant in composition, then one would expect it to return to a liquid state when the total pressure exceeded 35.7 mm. Hg. Tables III and IV demonstrate that not all of the gas disappeared until a total pressure in excess of 200 mm. Hg was achieved. One must conclude that at least some of the gas in the hand was not water vapor. One cannot be certain at this time whether the gas which originally formed was entirely water vapor or partly carbon dioxide and oxygen, with perhaps traces of nitrogen and argon.

Table V demonstrates that gas redeveloped in the hand at pressures far above the pressure needed to keep water in a liquid state at 32° to 36° C. One must conclude that the gas which redeveloped or re-expanded must not have been water vapor. In all probability the gas which expanded in the hand the second time it was exposed in glycerin was mainly carbon dioxide.

It is believed that the initial formation of the gas under the skin at 8 mm. Hg chamber pressure begins with the formation of a water vapor bubble. This bubble may be expected to come into equilibrium with both carbon dioxide and oxygen. Carbon dioxide is more soluble and diffuses more rapidly than oxygen and would be expected to reach a higher concentration in the bubble very quickly. On recompression to pressures much greater than 35.7 mm. Hg, the water vapor would be expected to return to a liquid state, leaving a bubble composed mainly of carbon dioxide and traces of oxygen. Subsequent reduction of the pressure about the hand would cause gas nuclei of carbon dioxide and oxygen to re-expand at pressures higher than the vapor pressure of water at 32° C.

Table VI demonstrates that there was no significant difference in the blood pressure recordings before and after the test. Two important factors operated during the incident described by Chubb (13) but not in this series. Kittinger's hand became swollen both because of gas formation at pressures less than 8 mm. Hg and because of the transudation of fluid across the great pressure head in the unprotected hand (68, 70). Also, Kittinger's hand was exposed to a low pressure for about 45 minutes, a longer exposure than any in this series. It is believed that factors other than those controlled in this series were probably responsible for the transient hypertension in Kittinger's right arm. It is also probable that the crepitus noted in Kittinger's hand at ground level was due to residual bubbles of carbon dioxide and oxygen. Carbon dioxide was probably the main cause of swelling observed by Henry and Wood.

The fact that there were no cases of dysbarism in this series suggests that nitrogen probably did not play an important role in the development of gas bubbles in these subjects. It is realized that it is sometimes possible to have nitrogen bubbles in the tissues without pain; however, cases of bubbles were all painless and all the bubbles resolved at pressures less than 750 mm. Hg chamber pressure.

Gas developed and disappeared in the human test subjects without causing temporary or permanent injury. This finding is in keeping with the experience of the other investigators.

Remarks

On first examination it might have seemed easier to maintain the denitrogenated subject in the chamber at 141 mm. Hg pressure and devise a large arm chamber capable of being evacuated to 3 mm. Hg. This idea was discarded mainly because the plethysmograph would have been less accessible for adjustments and because many tubes would have to penetrate the arm chamber. Work for the research team was facilitated by their having direct access to the plethysmograph.

For measuring the displaced volume of glycerin, both weighing and volumetric displacement seemed to be feasible methods. If displaced glycerin were caused by gravity to overflow into a container for weighing, it could be very accurately measured. Such a method is not reversible, however, since the glycerin will not flow backward without an elaborate hydraulic pressure system. This is the main reason why the volumetric method was chosen instead.

The original volumetric displacement method was designed to maintain a constant hydrostatic head of glycerin above the hand by raising and lowering the reservoir. With additional time this technic probably could have been perfected, but problems of a more strategic nature demanded attention. The difficulty in adjusting the reservoir arose from the limited hand motion of the subject in the pressurized pressure suit.

Another method of measuring the volume change of the hand could have been to immerse the hand in liquid wax of a tolerable temperature and to make replicas of the swollen hand. This method would not have given direct readout changes and would have been much slower.

An artifact in measuring hand volume changes was the apparent increase in volume seen when inflating the pressure suit or the pneumatic cuff. Several methods for solving this problem were available. In one instance the subject could be exposed to a very low chamber pressure with the suit and cuff inflated until the hand swelled. Then by adding known volumes of glycerin to the plethysmograph, the hydrostatic column could be greatly increased, thus repressurizing the hand while keeping the remainder of the subject and equipment unchanged. Such a system would require standpipes of an unwieldy length. It seemed more expedient, therefore, to measure the displacement caused by artifact during nonswelling and subtract it from the total displacement when swelling occurred.

If the standpipes had been replaced by fine-bore plastic tubing, the plethysmograph would have been much more sensitive to volume changes. Early tests with glass rods (1 mm. in diameter) demonstrated that larger-bore tubes would be more satisfactory since glycerin was displaced out of the tops of the long fine tubes.

There were no samples of gas taken from the pockets which formed on the hand. While this was a very tempting experiment, it was initially decided that a carefully planned and valid series of gas analyses could best be accomplished by a separate and distinct research task. Any future research into sampling and analysis of gas from human tissues exposed to low pressures should be preceded by appropriate studies on laboratory animals. Animal studies may be expected to yield valuable information which will help the research worker to perfect safe and reliable remote-sampling technics.

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

1. Gas initially develops in the ischemic hand exposed for 5 to 10 minutes at chamber pressures of 8 mm. Hg or less.

2. Once the gas develops, it disappears at total pressures in excess of 200 mm. Hg.

3. Gas develops in the hand on subsequent low-pressure exposure at total pressures of approximately 100 mm. Hg. The gas in the hand at this pressure is believed to be carbon dioxide with traces of oxygen.

4. The gas in the human hand varies in volume at specific total pressures. The volume of gas was observed to vary from 28 to 78 ml. at 50 mm. Hg total pressure.

5. A reliable plethysmograph was developed which could simply and accurately measure the changes in volume at any pressure greater than 1 mm. Hg.

6. Suitable roentgenographic technics were developed to demonstrate the formation of gas at very low pressures. Among the methods investigated, this technic was the most sensitive for detecting gas in the hand.

7. There was no significant change in the blood pressure of any subject subsequent to formation of gas in the hand.

8. In a three-month followup study there were no clinical indications of injury to the tissues nor of impairment of function of the hand.

Recommendations

1. A series of gas samples should be taken from the gas in the hand at various time intervals, for analysis. The following factors are important variables which should be carefully controlled: time of gas sampling; total pressure on the tissue; previous exposure of tissue to low pressure; tissue temperature; and denitrogenation of tissue.

2. A series of similar gas samples should be taken on perfused tissues from the limbs of animals. The samples should be taken while controlling the partial pressure of carbon dioxide and oxygen.

3. Connective-tissue pressures should be more adequately determined in the ischemic hand.

4. Investigation should continue to find a suitable substitute for glycerin, which is radio-opaque.

5. The present technics should be refined in order to perfect the sensitivity of the present plethysmograph.

The author expresses appreciation for the help of many people who assisted in this research project. Dr. H. G. Clamann and Dr. V. Montgomery offered many valuable suggestions as to the design of the plethysmograph. O. G. Langner assisted in the design and made all of the plethysmographic equipment. M. W. Jordan prepared the illustrations. Major Fritz M. G. Holmstrom and his staff and crews designed and built special equipment and operated the low-pressure chambers. S/Sgt. R. L. Hill and A/1C Leonard Harris were assistants to the investigator. Colonel G. L. Hekhuis and his staff monitored x-ray exposure and took all x-ray photographs. The author is especially indebted to the human volunteers.

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